in the N-termini segment. Hemichannel activity was evaluated by measure the plasma membrane permeability to fluorescent tracers, YO-PRO (MW 375.5 charge +2) and ethidium (MW 314.4; charge +1) and single channels conductances by whole cell patch clamp. Bathed in a divalent free cations solution HeLa cells expressing the syndromic G12R mutant show four and five folds increase in the uptake of YOPRO and ethidium, respectively, when compared to cells expressing wild type Cx26 (WT Cx26). At the single channel level, the full open state of the G12R mutant was around 600 pS; almost twice of the WT Cx26. On the other hand, the non-syndromic G12V and syndromic N14Y and S17F (most severe clinical phenotype) behave like the WT Cx26. These findings suggest that most Cx26 syndromic mutants in the N-termini mediate their pathogenicity by other mechanism than gain in hemichannel activity. Supported by: Millenium Institute-CINV, FONDECYT 1090573 and Anillo ACT-1104 to ADM; IEG is supported by CONICYT.

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Aging Restricts Electrical Signaling along Endothelial Tubes via Enhanced Activation of SK_{Ca}/IK_{Ca} Channels: Role for Oxidative Stress

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Electrical conduction in cellular networks is governed by gap junction patency between cells and the open state of membrane ion channels. In light of endothelial cell (EC) dysfunction with aging, we determined whether aging altered electrical signaling. Intact endothelial tubes (width: $\approx$60μm; length $\geq$ 2mm) isolated from superior epigastric arteries of Young (4-6 months) and Old (24-26 months) male C57BL/6 mice were studied using dual intracellular microelectrodes. Separation distance between sites of current injection and membrane potential (V_m) recording was 50-2000μm. A reduction in electrical length constant (Δ) from 1630 (Young) to 1320μm (Old) accompanied an increase in restingV_m from Young (-28 ± 1mV) to Old (−36 ± 1mV) (n≥9; P<0.05). With similar pEC_{50} values and maximum V_m responses to acetylcholine (ΔV_m Young: 7.3 ± 0.1, −38 ± 3mV; Old: 7.2 ± 0.1, −39 ± 1mV), the conduction amplitude (CA; ΔV_m/nA current injection) for intercellular electrical signaling was less (P<0.05) in Old vs. Young (at 500 μm: 5.9 ± 1 vs. 8.9 ± 1 mV/nA; n=6). Despite similar hyperpolarization (~-35 mV) to direct activation of calcium-activated K^+ channels (SK_{Ca}/IK_{Ca}; $K_{Ca}2.3$ and $K_{Ca}3.1$) with NS309 (1μM), the reduction in CA was greater (P<0.05) in Young vs. Old (−6 ± 1 vs.-4 ± 1 mV/nA; n≥7). Inhibiting SK_{Ca}/IK_{Ca} (apamin+charybdotoxin) restored conduction in Old to that of Young (at 500 μm:~10 mV/nA; n=6). To investigate a role for oxidative stress, H_2O_2 (200 μM) increased V_m to E_K (≈-90mV) and impaired CA by ≥ 90% (n=8) in Young; these effects were blocked by apamin+charybdotoxin (n=6). Catalase (500 U/ml) depolarized resting V_m from −38 ± 1 to −28 ± 1mV and increased CA by ≈30% in Old (n=7; P<0.05). Thus restricted spread of electrical signals along endothelium of Old reflects enhanced current dissipation through open SK_{Ca}/IK_{Ca} in response to oxidative stress. (Support: NIH R01-HL086483, R37-HL041026, F32-HL110701)

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Petal Thicknesses and Shape Transformations in Blooming Lilies

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During blooming, flower petals undergo significant shape changes. For lilies, various different mechanisms responsible for the change have been suggested [1,2]. One is that cell growth along the edge of a petal, or, more generally, a tepal, drives a transition from a cup shape (within a bud) to a saddle shape (within a bloom). This mechanism has been previously considered for tepals modeled as shallow elliptical shells whose thickness from the center, t, falls off at least as fast as $t = t_0 (1 - x^2/a^2 - y^2/b^2)$ [1]. Here t_0 is the maximum thickness of the shell, a and b are the semimajor and semiminor axes, x and y are the coordinates along the longitudinal and lateral axes. By measuring tepal thicknesses from images collected by x-ray tomography of intact buds and by photography of microtomed buds, we find that this condition is indeed met for both *Lilium casablanca* and *Lilium lancifolium.*

Figure: Two open lily flowers

[1] Liang and Mahadevan. Growth, geometry, and mechanics of a blooming lily. PNAS, 108:5516-5521, 2011.
[2] Bieleski et al. Mechanical Aspects of Rapid Flower Opening in Asiatic Lily. Annals of Botany, 86:1175-1183, 2000.

2519-Pos Board B538

Adaptation Rates of E. Coli in Monovalent Salt Solutions

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A complete description of bacterial populations requires a large-scale model of how populations adapt to their environment. In this study we start with a bacterial pre-culture that has been grown in LB (Lennox Formula) broth and use 500 μL aliquots of preculture to grow *E. coli* colonies in a shaker at 37°C and ~300rpm. These experiments are conducted in 500 mL Erlenmeyer flasks with a working volume of 125 mL and cell density is measured by optical density at 600 nm. In concentrated monovalent salt solutions, *E. coli* growth rate is affected by both the positive and the negative ions. For both chloride and bromide salts, we obtain the toxicity sequence K > Na >Li. Comparing the effect of anions, we find that bromide salts are more toxic than chloride salts. For adaptation studies to environmental stress, we use either 500 mM NaCl or a temperature shift from 37 to 41.5°C. Adaptation at the population level is marked by a sudden increase in population growth. We discuss the observed timescale of the adaptation process and its functional form which are useful for constructing mathematical models for bacterial populations.

2520-Pos Board B539

Noise Propagation through Cytokine Signaling Leads to Fluctuations in Interferon-Induced Genes

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We propose a general mechanism whereby fluctuations in cytokine production can cascade through inter-cellular diffusion to downstream induced genes. We thus highlight the importance of inter-cellular signaling in cell-to-cell variability. We simulate an agent-based model in two dimensions, which provides a mechanistic understanding of noise propagation through inter-cellular communication, and establish conditions under which the mechanism is operative. We illustrate it in the context of experiments on human dendritic cells infected with Newcastle Disease Virus, a non-pathogenic virus that shows large cell-to-cell variability of the interferon-induced gene DDX58. The stochastic induction of interferon-β itself leads to large spatial heterogeneity in the secreted cytokine at early times after infection; this heterogeneity results in large spatial variability in the bound receptors that induce the Jak-Stat pathway and therefore in the genes induced by the signaling. Our results give insight into the impact of spatial and temporal heterogeneity on autocrine and paracrine signaling in a collection of cells. We find that autocrine signaling is important immediately after IFNβ induction starts but eventually paracrine signaling dominates promoting spatial homogeneity.

Computational Systems Biology

2521-Pos Board B540

A Programmatic Modeling Approach to Explore Alternative Hypothesis of Mitochondrial Regulation in Extrinsic Apoptosis Signaling

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Experiments often result in observations that can lead to conflicting interpretations of biochemical mechanisms in signaling networks. We aim to use mathematical modeling of extrinsic apoptosis signaling networks to address such experimental observations and provide a theoretical explanation to seemingly discordant interpretations. Probing multiple mechanistic hypotheses in biological modeling often involves the instantiation of complex systems of equations, which despite their usefulness can make model revision, extension, and sharing extremely challenging. To address these modeling barriers, we have developed a modeling framework that allows biological models to be written as native Python programs that encode biological functions. Our modeling framework, PySB, offers access to a large set of existing numerical and programming methods to biological systems modeling. We discuss the implementation of our approach and show how it can be used to explore multiple hypotheses to describe the regulation of mitochondrial outer membrane permeabilization among the Bcl-2 family of proteins. We use our modeling framework to systematically explore proposed mechanisms, both from the literature and from our own experimental work, resulting in the instantiation, comparison, and calibration of multiple model topologies for numerical exploration. Our preliminary results, based on simulations calibrated to experimental data, suggest that the so-called indirect mechanism does not accurately reproduce experimental